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| 09/851,071      | 05/08/2001  | Ann Marie Schmidt    | 0575/55424-Z/JPW/SHS/MVM | 3248             |

7590 12/01/2005  
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EXAMINER

KAUSHAL, SUMESH

ART UNIT PAPER NUMBER

1633

DATE MAILED: 12/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/851,071

**Applicant(s)**

SCHMIDT ET AL.

**Examiner**

Sumesh Kaushal Ph.D.

**Art Unit**

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2005.  
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 17,19,20 and 35 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 17,19,20 and 35 is/are rejected.  
7) ☒ Claim(s) 41-43 is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.  
5) ☐ Notice of Informal Patent Application (PTO-152)  
6) ☐ Other: \_\_\_\_\_.

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### ***DETAILED ACTION***

*Claims 17, 19-20, 35 and 40-43 are pending and are examined in this office action.*

*Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300.*

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/12/05 has been entered.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 17, 19-20, and 40 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 57-60 and 76-78 of copending Application No. 09/689,469. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of a method for evaluating the ability of an agent that inhibits tumor spreading by contacting tumor cells in a cell culture with an agent that inhibits the binding of RAGE on tumor cells with a matrix coated amphotericin as claimed in the instant application is identical to the scope of a method of identifying an agent which inhibits tumor invasion by contacting tumor cells expressing RAGE with a solid support coated with amphotericin in the presence of candidate agent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Claim Rejections - 35 USC § 103***

Claims 17, 19-20 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gehlsen et al (JCB 106:925-930, 1988, *ref of record*) in view of Hori et al (JBC 70(43):25752-25761, 1995, *ref of record*) and Miki et al. (Biochem Biophys Res Commun 196(2):984-9, 1993).

The invention as claimed is drawn to a method for evaluating the ability of an agent to inhibit tumor cell spreading, wherein the agent inhibits the interaction between RAGE on tumor cell and an extra cellular matrix molecule (i.e. amphotericin).

Gehlsen teaches inhibition of in-vitro tumor cell invasion by Arg-Gly-Asp- (RGD) containing synthetic peptides. Regarding claim 17 the cited art teaches that for the invasion assays the synthetic candidate polypeptides were dissolved in DME (cell culture media) with 2% FBS, 0.1% Gentamycin and 10mM Hepes buffer. The cited art

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further teaches that for cell attachment assay the peptides were dissolved in same media expect the serum was omitted (page 926, col.1 para.4). The cited art further teaches that tumor cells were cultured in DME culture media supplemented with 10%FBS and 0.1% gentamycin (page 926, col.1 para.1). The cited art further teaches the attachment of purified extracellular matrixes (i.e. Fibronectin and Vitronectin) to the polystyrene culture dishes (page 926, col.1 para. 2). The cited art further teaches evaluation of invasiveness of tumor cells using a membrane invasion culture system (MICS). The tumor cells (A375 melanoma, RuGli glioblastoma) were pre-incubated and cultured into upper compartment of the MICS chamber followed by addition of peptide-containing medium (page 926, col.2 para.1, fig-1). The cited art teaches that at specific time intervals after the addition of the candidate peptide the medium from upper and lower compartments of the chamber was removed and total number of cells that passed though the membrane was evaluated (page 926, col.2 para.1, fig-1). The cited art further teaches microscopic evaluation of spreading of tumor cells in the presence of absence of candidate agents (page 926, col.2 para.2). Regarding claims 19-20 the cited art teaches metastatic melanoma cells (A375m, A375P) and RuGli glioblastoma cells (page 926, clo.2 para.3). The cited art further teaches that the MICS membrane invasion culture system used herein comprises a human amniotic basement membrane (denuded of cells), which express extracellular matrix proteins laminin, type IV collagen, fibronectin and vitronectin (page 929, col.1 para.1-3, col.2 para. 4, page 925, col.1-2). In addition the cited art further teaches the attachment of purified extracellular matrixes (i.e. Fibronectin and Vitronectin) to the polystyrene culture dishes (page 926, col.1 para. 2)

Even though the Gehlsen teaches a method for evaluating tumor invasion the cited art does not specifically teach the evaluating the ability of an agent that inhibit tumor cell spreading by inhibiting interaction between RAGE on tumor cells and Amphoterin.

Hori teaches that the RAGE is a cellular binding cite for Amphoterin. The cited art further teaches a method of inhibiting the binding of amphoterin to RAGE by incubating an agent, sRAGE or soluble RAGE, to plates coated with amphoterin. The cited art

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further teaches that this method is used to identify the amount of cell growth inhibited by sRAGE (page 2578, fig-5). The cited art further discloses the role of amphoterin/RAGE interaction for the invasiveness of neoplastic lesions (pg 25760 column 2). Even though Hori does not disclose expression of RAGE especially on tumor cells, it has been well known in the art that the tumor cells inherently express RAGE which is associated with cellular growth (see Miki et al, page 984).

Thus it would have been obvious to one ordinary skill in the art at the time the instant invention was made to modify the invention of Gehlsen by evaluating the ability of an agent that inhibits the interaction between RAGE expressed on tumor cells and Amphoterin in view of Hori and Miki. One would have been motivated to do so identify candidate agents to inhibit tumor metastasis. One would have a reasonable expectation of success, since evaluation of a candidate compound that inhibit extracellular-matrix/tumor-cell interaction using a tumor attachment assay or a tumor invasion assays had been routine in the art the time the instant invention was made. Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

### **Conclusion**

Claims 17, 19-20 and 40 are rejected.

Claims 35 and 41-43 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten independent form including all of the limitation of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547**. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**.



**SUMESH KAUSHAL  
PRIMARY EXAMINER  
ART UNIT 1633**